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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,954	10/21/2008	Beverly L. Davidson	17023.045US2	4645

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,954	DAVIDSON ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *82-119* is/are pending in the application.

4a) Of the above claim(s) *109-119* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *82-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/06,4/25/06,5/04/06,7/7/06,8/2/06,9/8/06,11/22/06,11/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 82-108, pol II and AAV vector, in the reply filed on 02/04/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of the Application

Claims 82-119 are pending. Claims 82-108 are currently under examination. Claims 109-119 and non-elected inventions are withdrawn as being drawn to a non-elected invention.

Information Disclosure Statement

The submission of the Information Disclosure Statements on 04/03/2006, 04/25/2006, 05/04/2006, 07/07/2006, 08/02/2006, 09/08/2006, 11/22/2006 and 11/23/2007 is in compliance with 37 CFR 19.7. The information disclosure statements have been considered by the examiner and signed copies have been placed in the file.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 82-108 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-61 of copending Application No. 11/597,225. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are encompassed in the claims of copending application 11/597,225.

The instant claims are drawn to a mammalian cell comprising a siRNA targeted to a nucleotide sequence encoding a mutant Huntington's Disease protein wherein the mammalian cell comprises an AAV vector, wherein the vector comprises a pol II promoter, a marker and a polyadenylation signal.

Claims 1-61 of copending Application No. 11/597,225 are drawn to an isolated RNA duplex wherein the first strand comprises at least 15 contiguous nucleotides of SEQ ID No. 68, wherein the isolated duplex is in an expression cassette, wherein the expression cassette is in an adenoviral vector, wherein the siRNA is targeted to Huntington's Disease gene and wherein the siRNA comprises overhang regions and a loop structure and therefore claims 1-61 encompass claims 82-108 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 82-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boado et al. (of record Applicant's IDS filed 04/03/2006), Partridge et al (US 2003/0165853 of record Applicant's IDS filed 11/23/2007), Tuschl et al. (US 2002/0086356 of record Applicant's IDS filed 04/03/2006), Engelke et al. (US 2003/0148519 of record Applicant's IDS filed 07/07/2006), Wands. (US Patent No. 6,001,990 of record Applicant's IDS filed 04/03/2006) and Patel et al. (US Patent No. 6,420,345 of record Applicant's IDS filed 04/03/2006).

The instant claims are drawn to, a mammalian cell comprising a first and second strand of 15 to 30 nucleotides wherein the first strand comprises at least 12 nucleotides complementary to a nucleotide sequence encoding a mutant Huntington's Disease protein, wherein the siRNA comprises a overhang region, wherein the siRNA forms a hairpin structure comprising a duplex structure and a loop structure, wherein the vector is AAV and comprises a pol II promoter, a marker and a polyadenylation signal.

Boado et al. teach Huntington's disease is an autosomal dominant neurodegenerative disorder that causes impairment of cognitive and motor functions and severe neuronal loss (see page 239). Boado et al. teach the mutation underlying the disease is an expansion of a trinucleotide repeat region of the gene coding for the huntingtin protein and demonstrated antisense compound targeted to the Huntington's gene was able to reduce expression of the huntingtins protein (see page 239 and Table 1). Boado et al. teach decreasing the expression of the huntingtins protein in cell lines allows one to investigate the etiology of the disease and develop potential therapeutics (see page 242). Boado et al. do not teach siRNA targeting a Huntington's gene and do not teach expression vectors comprising regulatable or a constitutive promoters or hairpin siRNA comprising loops structures of 4 to 10 nucleotides.

Partridge et al. teach antisense oligonucleotides that specifically target, hybridize and inhibit expression of the target human Huntingtin gene in vitro and in vivo (abstract, p. 10, at 0109- p. 11 at 0122, example 2 on p. 17 at 0179 – p. 20 at 0211, and tables 1 and 2 and text on p. 21).

Tuschl et al. teach the use of a more efficient nucleic acid to inhibit gene expression wherein the nucleic acid is comprises of a dsRNA structure. Tuschl et al. teach inhibition of expression of the marker gene luciferase using siRNA duplexes between 19-25 nucleotides in length, and optionally further comprising 5' and/or 3' overhangs comprising between 1 and 10 nucleotides (see p. 8, figure 14b, pages 10, 27 and 28). Tuschl et al. teach how to make and use siRNA targeted to any target gene in cells such as mammalian cells.

Engelke et al. teach the use of a siRNA expression vector for expressing a hairpin RNA comprising a loop structure (see Figure 1A) wherein the hairpin RNA comprises a first, second and third region wherein the first and third region are complementary to each other having 18 to 25 nucleotide pairs and the second region is between each of the first and second region and forms a loop of about 4 to 10 nucleotides in length (see page 2, particularly paragraphs 0011-0017 and pages 1, 9 and 10). Engelke et al. teach the transcribed RNA duplex is targeted to and inhibits expression of a target gene Lamin A/C (see Figure 6 and paragraph 003). Engelke et al. teach the siRNA contain 3' overhangs of 2 to 4 nucleotides (see paragraph 0105) and teach the expression vector comprises constitutive or regulatable promoters, marker genes and the use heterologous minimal SV40 polyadenylation signals (see pages 9 and 10).

Wands et al. teach AAV expression vectors comprising molecules that specifically target and inhibit the expression of a gene of interest, which vectors optionally comprise constitutive or regulatable promoters, including RSV promoter containing viral vectors (col. 2-4, 5-7).

Patel et al. teach AAV expression vectors for expression of heterologous nucleic acids in target cells, and which expression vectors comprise appropriate and operably linked promoters (including but not limited to the CMV and H6 promoters) and which expression vectors further comprise polyadenylation signals and optionally comprise a selectable marker gene (see col. 1-4, 13-16, figures 2, 3, 8, 12 and 13).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the methods taught by Tuschl et al. to make a siRNA targeted to a Huntington's gene as taught by Boado et al. and Partridge et al. It would have further been obvious to express said siRNA in expression vectors as taught by Engelke et al. and express said siRNA with a viral vector such as an AAV-1 vector, as taught by Wands et al. and Patel et al. to deliver said vector to cells for the treatment of such a disease.

One of ordinary skill in the art would have been expected to be able to design any siRNA targeted to any mRNA transcript because Tuschl et al. details the steps to effectively find a target site in any RNA and design and test siRNA molecules for specific RNAi activity. Given that Boado et al. identified sequences responsible for expression of mutant huntingtin protein and has shown that this protein plays a critical role in the progression of Huntington's disease.

One of skill in the art would have wanted to express the siRNA using the expression vector taught by Engelke et al. given Engelke et al. teach said expression vector efficiently expressed the RNAi molecule in mammalian cells for longer periods of time. Further, one would have wanted to express siRNA or shRNA using an AAV-1 vector because AAV-1 vectors were well known in the art and the skilled artisan would have been motivated to use an AAV-1 vector to express a therapeutic nucleic acid given that Xiao et al. teach AAV vectors are not associated with any known disease and are not considered pathogenic and further, AAV-1 vectors are preferred over the other subtypes.

Finally, one of ordinary skill in the art would have expected to be able to generate a siRNA targeted to a Huntington's gene given Tuschl et al. teach the basic steps to identifying any target site and screening siRNA molecules for activity and given Boado et al. and Partridge et al. has identified specific sequences that express proteins that are involved in the progression of the Huntington's disease, one of ordinary skill in the art would have expected to be able to make siRNA targeted to these regions. One would have had a reasonable expectation of success at expressing a first strand or a second strand of an siRNA from an expression vector given Engelke et al. teach construction of such expression vectors of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Fereydoun Sajjadi at 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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